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WHEN A RARE VERTEBRAL ARTERY PSEUDOANEURYM COMPRESSES THE BRAIN STEM – IS REFERRAL THE ONLY SOLUTION FOR NEUROLOGISTS OR CAN NANOPHARMACOLOGY OFFER HELP IN FUTURE?

Monika Sachan[1], Suman Kushwaha[2], Shah Faisal Ahmad Tarfarosh[3], Mohammad Faizan Bhat*[4], Atul Yadav[1], Ashutosh Gupta[1] and Mushbiq Manzoor[5]

[1]Senior Resident, Institute of Human Behaviour and Allied Sciences, Dilshad Garden, Delhi, India, 110095.
[2]Associate Professor and HOD, Institute of Human Behaviour and Allied Sciences, Dilshad Garden, Delhi, India, 110095.
[3]Clinical Fellow, Division of Medical and Surgical Neurosciences, Salford Royal Hospital, Manchester, United Kingdom, M6 8HD.
[4]Department of Pharmaceutical Sciences, University of Kashmir, Srinagar, Jammu and Kashmir, 190006.
[5]Resident, Institute of Human Behaviour and Allied Sciences, Dilshad Garden, Delhi, India, 110095.

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***Corresponding Author**
Mohammad Faizan Bhat
Department of Pharmaceutical Sciences, University of Kashmir, Srinagar, Jammu and Kashmir, 190006.

ABSTRACT

It is very rare to have a Pseudoaneurysm of vertebral arteries, especially without any traumatic event. Only few such cases have been reported till date. We report one such case in which the vertebral artery aneurysm was compressing the brainstem. We also review the medical literature regarding the futuristic role of nanomedicine in the hands of neurologists in such cases rather than time consuming referral to other departments.

KEYWORDS: Pseudoaneuryms, brain-stem compression, neurology, neurosurgery, Neuroradiology, nanotechnology.

INTRODUCTION

Pseudoaneurysm of the vertebral artery is extremely rare and usually occurs after penetrating or blunt trauma. Injuries of these arteries are less common as compared to extra cranial carotid artery because of their anatomic location along the Vertebrae. The natural history of the vertebral artery pseudoaneurysm is not yet well defined because very few cases have been

reported to date. The clinical presentation may vary depending upon the site of an aneurysm and its sequela. Here, we report a case of idiopathic pseudoaneurysm of v4 segment of vertebral artery arising just proximal to origin of basilar artery presenting to us as brain stem compression symptoms.

CASE REPORT

An 18 yr old male presented to us with a chief complaint of severe neck pain with an occipital headache and vomiting (increased in early morning) for eight months, weakness of right upper and lower limb for six months, dysphagia for both solid and liquids along with nasal regurgitation and choking episodes for five months, and slurring of speech with nasal intonation for four montha. There was no history of head and neck trauma, any surgical intervention, or vigorous neck massage. On examination, vitals were stable, GCS 15/15, cranial nerve examination showed horizontal gaze-paretic nystagmus along with upbeat vertical nystagmus bilaterally, trigeminal reflex was absent, gag reflex was absent, and uvula is central. Motor examination showed hypertonia and power was 3/5 in both right upper limb and lower limb. Deep tendon reflex was brisk in all four limbs with plantars bilateral extensor.

Computerised tomographic (CT) angiography of head and neck showed a complex vertebral artery aneurysm involving the intradural segment (v4 segment) on the right side. There was also evidence of well defined peripheral crescent of increased attenuation within the thrombus of the large vertebral artery aneurysm suggestive of impending rupture of the same. Aneurysm was completely filling the prepontine cistern and foramen magnum and causing mass effect over the pons and adjoining structures. Moderate dilation of both the lateral ventricles and the third ventricle was noted. Also, fourth ventricle is compressed, suggestive of non communicating hydrocephalus (Obstructed hydrocephalus).

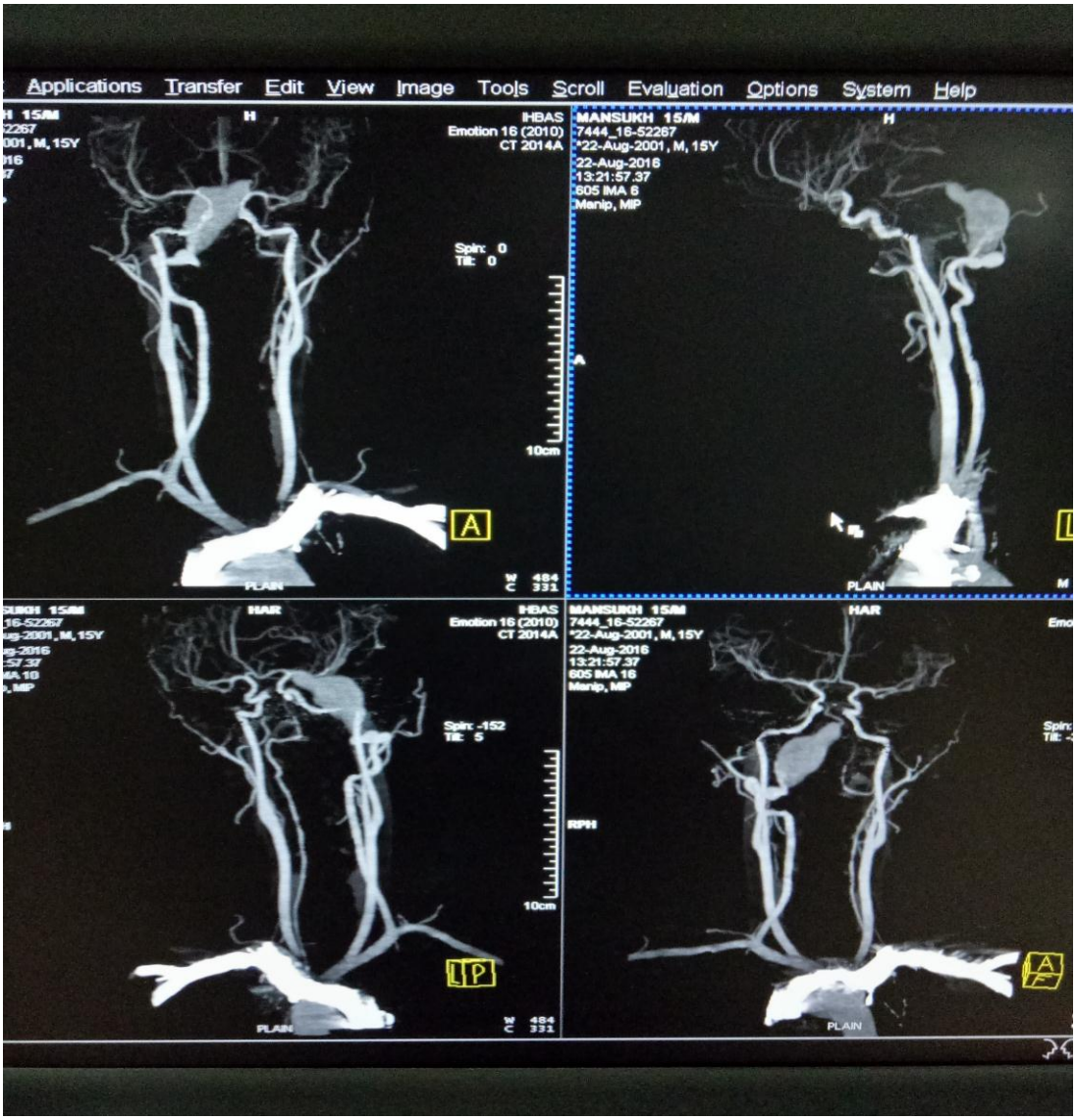
Insert Figures 1a-b and 2 here

We discussed this case with neurosurgeon and interventional radiologist.Gold Bal Ballon occlusion of right vertebral artery was done by neuroradiologist. Left high pressure Ventriculo-peritoneal (VP) shunting was done by the neurosurgeon. Patient showed considerable improvement on follow up after 1 month.

DISCUSSION

Vertebral artery pseudoaneurysm is a rare entity.Pseudoaneurysms typicallylack a true wall and are covered by a friable layer of connective tissue. They are usually developed after penetrating wounds, Percutaneous angiography,pathologic fracture or dislocation of cervical vertebrae caused by arthritis, chiropractic manipulation, head injury and neck trauma and a few more clinical conditions[1-3].

Atraumatic aneurysms are less frequent. Such lesions are caused by inflammatory processes, such as staphylococcal osteomyelitis, endarteritis, necrotizing arteritis, and other connective tissue disorder. Spontaneously dissecting vertebral artery aneurysm has also been described. Some congenital extracranial vertebral aneurysms are associated with inherited disorders, such as the Ehler-Danlos syndrome, neurofibromatosis, and fibromuscular dysplasia[4-6].



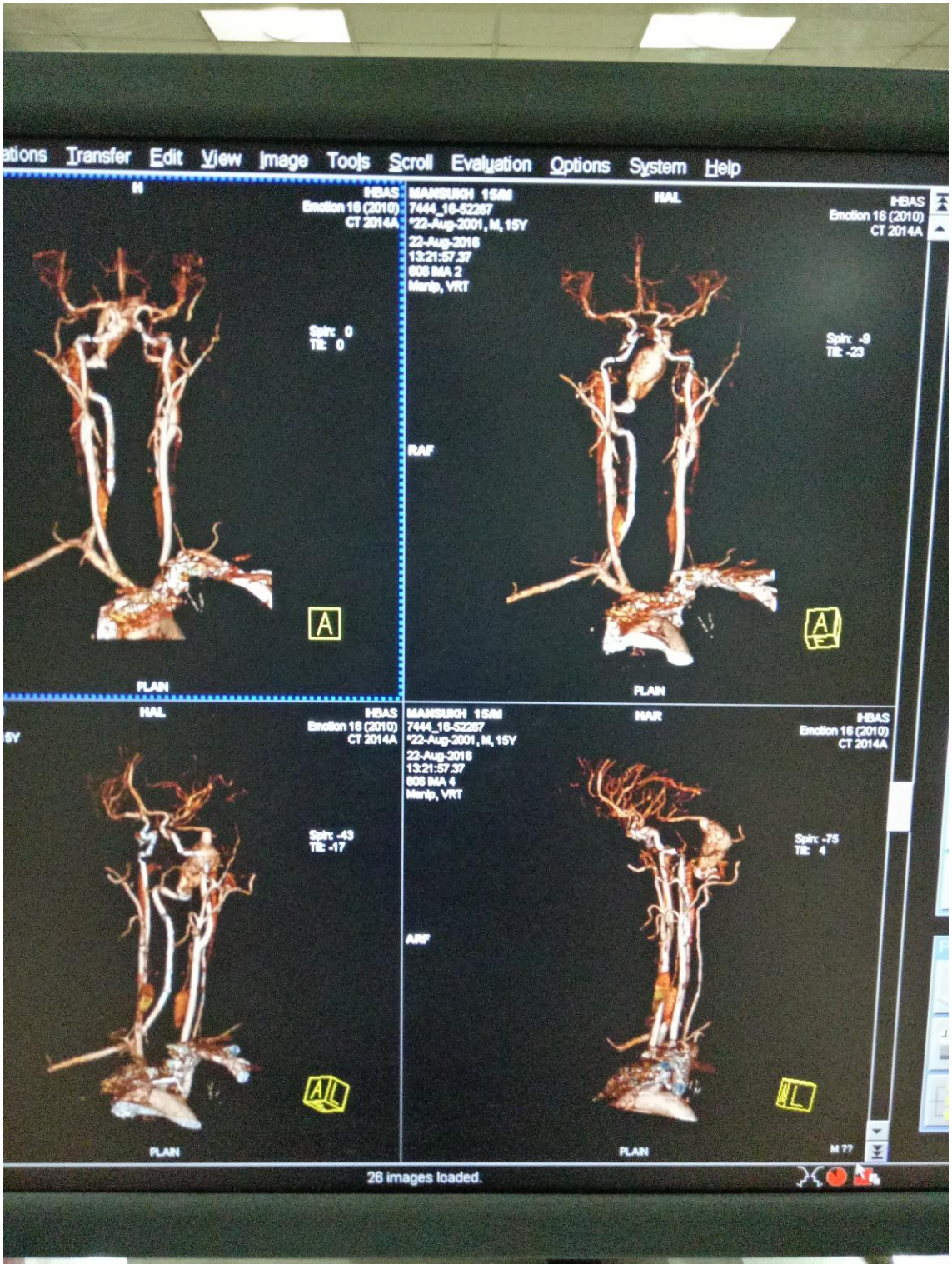


Figure 1a, 1b. CT angiography of head and neck show a complex vertebral artery aneurysm involving the intradural segment (v4 segment) on the right side. There is also evidence of well defined peripheral crescent of increased attenuation within the thrombus of the large vertebral artery aneurysm suggestive of impending rupture of the same.

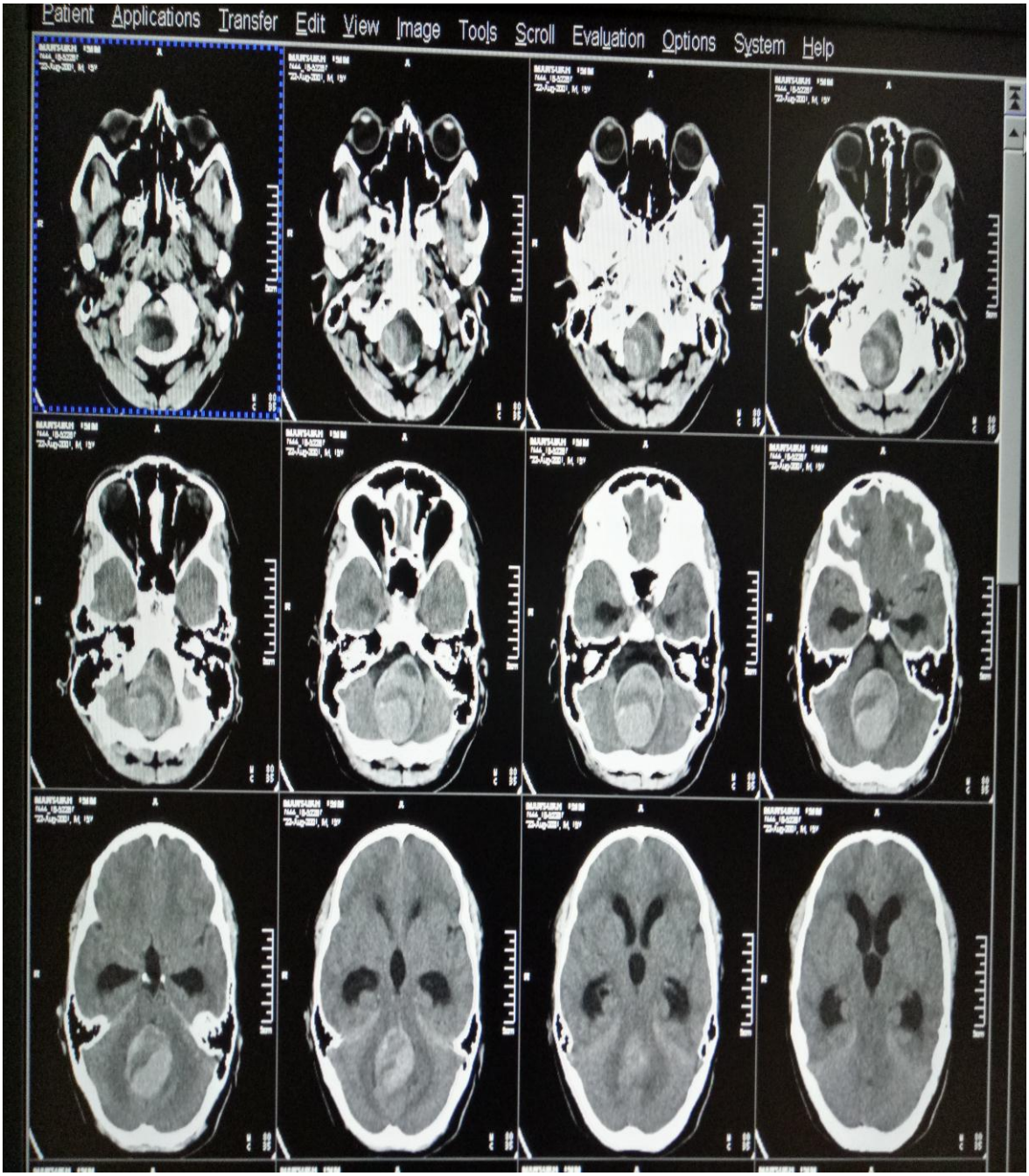


Figure 2. Aneurysm is completely filling the prepontine cistern and foramen magnum and causing mass effect over the pons and adjoining structures. Moderate dilation of both the lateral ventricles and the third ventricle are seen. Also, Fourth ventricle is compressed, suggestive of non communicating hydrocephalus (Obstructed hydrocephalus).

There are a few reports in the world literature of intracranial vertebral artery aneurysm of atraumatic origin.[7-10] Usually Intracranial vertebral artery aneurysm has three clinical manifestations: ischemia, hemorrhage, and mass effect. A chronic, giant, dissecting

aneurysm can cause mass effect on the brain stem or cranial nerves, as well as distal embolism. Pseudo aneurysms of V3 or V4 segment of vertebral arteryare usually presented with intracranial haemorrhage[11].

According to various sources[12-14] treatment of vertebral artery pseudoaneurysms patients must be decidedon individual basis and also depends on size, location, site ofaneurysm. Endovascular intervention is probably best applied in patients who have small aneurysms with or without arteriovenous fistula. Aneurysms in the 3rd and 4th portion of the artery are the most difficult to treat.Brainstem compression by vertebral artery (VA) aneurysm is extremely rare and only reported in a few cases[15]. The case presented to us was with bulbar palsy and symptoms of raised intracranial tension due to compression of brainstem by giant pseudo aneurysm of vertebral artery without history of trauma.

Although the case was treated by surgical procedures, there might be a better scope for therapeutics to treat aneurysms for better patient compliance and faster treatment without the intervention of a neurosurgeon or neuroradiologist. But, there are many problems associated with targetting drugs to the diseased vessel walls, this is mostly because of the high shear flow conditions in arteries, parenteral, oral environments and the fact that intra-arterial administration of therapeutics have limited access and often lead to unwanted systemic side effects[16]. Therefore, new strategies have been developed for targetted and effective drug delivery to vascular sites and these approaches use various underlying markers of the vasculature for meticulous drug delivery. Nanomedicine is on the forefront of such approaches, with an abundant literature suggesting a variety of nanotechnological methods to tackle wholely or in part the complications of vascular aneurysms. Of these, some of the most important have been collected.

Liposomes. Liposomes are lipid bilayer self-assembling vesicles with a diameter ranging from 20 to150nm for Small Unilamellar Vesicles (SUVs) to a few micrometers in diameter for Large Multicellular Vesicles (LMVs). Plenty of studies suggest the use of liposomes and their effectivity in passive as well as active targetted therapeutic applications[17,18]. Liposomes have a tremendous potential for surface-modifications and drug encapsulation and it is mostly these two main reasons why they have been successfully employed for vascular disease-targeted gene delivery[19-23]. Actively targetted echogenic liposomes have been designed and reported to enhance ultrasound imaging quality of atheroma in a Yucatan miniwise model[24, 25]. And this approach has been further developed and used by various researchers to deliver

thrombolytic/fibrinolytic agents (e.g., tPA) to the desired site[26]. Computed Tomography (CT) agents (e.g., iohexol) and MRI agents (eg., Gadoteridol) have also been included in liposomes with positive *in vivo* results in rabbits[27].

Micelles. A micelle is another form of the nanostructure with a hydrophilic shell and a hydrophobic core. Various studies have used and reported positive delivery of therapeutics as well as contrasting agents to the desired vascular site[28-34].

Polymer NanoSpheres and Nanoshells/capsules. Polymers have been revered in biomedical sciences more than any other material, this is especially because of their biocompatibility, biodegradability and the ability to be precisely tuned and tailored according to the physiochemical and mechanical needs. It is, therefore, no surprise that these materials have also made it in the vascular aneurysms and other vascular disorders. Reports of these materials being used for vascular disease go back as far as about 20 years[34-36], and because of all their advantages, their use have been evaluated and positively reported over the course of time[35-42].

Ultrasound-Sensitive nanostructures. UltraSound (US) based imaging materials and techniques have been long known and used for diagnosis and detection of pathological and physiological tissues and therefore a lot of research has been carried out on this approach for targetted molecular vascular imaging of the diseases[43-47].

Dendrimer Nanostructures. Dendrimers are a globularly conformed novel class of material that consist of highly branched or cascade polymers. In the vascular context, dendrimers have been mostly used and studied for loading and delivery of imaging probes (e.g., MRI)[48-54].

Magnetically Sensitive Nanostructures. Magnetically Sensitive Nanostructures share the stage with some of the most researched nanoparticles because of their capacity to be modified for better cell-selectivity and disease-site selectivity and then guiding their localization to the desired site using magnetic fields and using their intrinsic properties to obtain spatiotemporal and anatomic information of the disease. This has eventually lead to development of copious amount of techniques and materials for imaging contrast that eventually lead to better and prompt diagnosis[55-61].

Nanorobots. A Nanorobot is one of the most novel technique that has gained and continues to gain research interest and exposure because of the enormity of its applications, especially in

the field of medicine. Quite a few articles suggest and propose how nanorobotics should help with early detection of cerebral and other forms of aneurysms[62-65].

To conclude, it is strongly clear from the above discussion and discourse that aneurysm should be taken care of, without discriminating between approach, be it the traditional surgical intervention or the more promising, more agile and more rewarding nanopharmacological, nanomedical and even nanoelectronic slant. Some interventional neurologists have replaced the need of endovascular or neuroradiologic interventions by getting trained in many invasive procedures. So, it is essential that the future neurologists, as well as cardiologists, lessen the burden on their counterparts as well as deliver a more futuristic promising treatment to such patients, by looking forwards to research and getting trained in nanomedicine, especially for such life threatening aneurysms.

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